HETEROCYCLES, Vol. 80, No. 1, 2010, pp. 379 - 393. © The Japan Institute of Heterocyclic Chemistry
Received, 9th June, 2009, Accepted, 31st July, 2009, Published online, 5th August, 2009
DOI: 10.3987/COM-09-S(S)33

CHEMO- AND REGIOSELECTIVE IMINO DIELS-ALDER REACTIONS: SYNTHESIS OF FUNCTIONALIZED NOVEL QUINOLIN-3-ONE AND QUINOLINE DERIVATIVES

Chander Mohan, Gaurav Bhargava, and Mohinder P. Mahajan*

Department of Applied Chemistry, Guru Nanak Dev University, Amritsar – 143005, Punjab, India. Fax +91(183)225881920; E-mail: mahajanmohinderp@yahoo.co.in

Abstract – Regio- and catalyst selective imino Diels-Alder reactions of vinyl/isopropenyl pyrimidinones with *N*-arylimines in the presence of metal salts *viz*. magnesium(II) bromide, zinc(II) chloride, indium(III) chloride, yttrium triflate and scandium triflate, are described. An unprecedented oxidation of methylene to carbonyl has been shown to accompany the imino Diels–Alder reactions of isopropenyl pyrimidinones in the presence of yttrium and scandium triflates. Chemoselective effect of different Lewis acids used as catalysts in these reactions has been rationalized.

INTRODUCTION

The imino-Diels-Alder (IDA) reaction involving the coupling of imines, derived from aromatic amines, or their surrogates,[1] with electron rich alkenes has emerged as a powerful tool for the synthesis of tetrahydroquinolines[2] and allied substrates. Some of these substrates are known for their biologically latency *viz.* psychotropic, antiallergic, anti-inflammatory and estrogenic activities.[3] There are numerous reports on the IDA reactions of *N*-arylimines with sterically unhindered activated alkenes, cyclopentadiene or symmetrical activated butadienes catalyzed by a variety of metal salts and protic acids.[4, 5] Such reactions suffered from lack of chemoselectivity and resulted in formation of a mixture of adducts.[4] However, the reports concerning the use of acyclic un-activated and sterically hindered alkenes as dienophiles in such IDA reaction are rare.[5]

In recent communications, we have compared the dienic properties of *N*-arylimines in their Lewis acid mediated cycloaddition reactions with 5-isopropenyl pyrimidinones and 3-dienyl-2-azetidinones (Figure

1). These reactions were shown to result in the formation of 5-quinoline substituted pyrimidinone/azetidinone derivatives with participation of *N*-aryl imines as 4π component of 2-azadiene.[6a, 6c] In continuation of these studies, we report herein a detailed account of chemo- as well as regioselective metal salts or Lewis acid catalysed IDA reactions of 5-isopropenyl/vinyl pyrimidinones with *N*-arylimines. Interestingly, these reactions resulted in a catalyst selective formation of novel pyrimidinone tethered quinoline, dihydroquinoline and quinolin-3-one derivatives depending upon the nature of the metal salts or Lewis acid employed. Such functionalized pyrimidinones have been reported to show antitumour, antiviral, antitubercular, antifungal, molluscidal and larvacidal activities.[7]

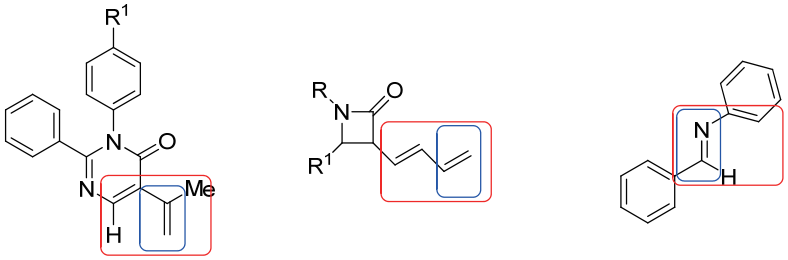


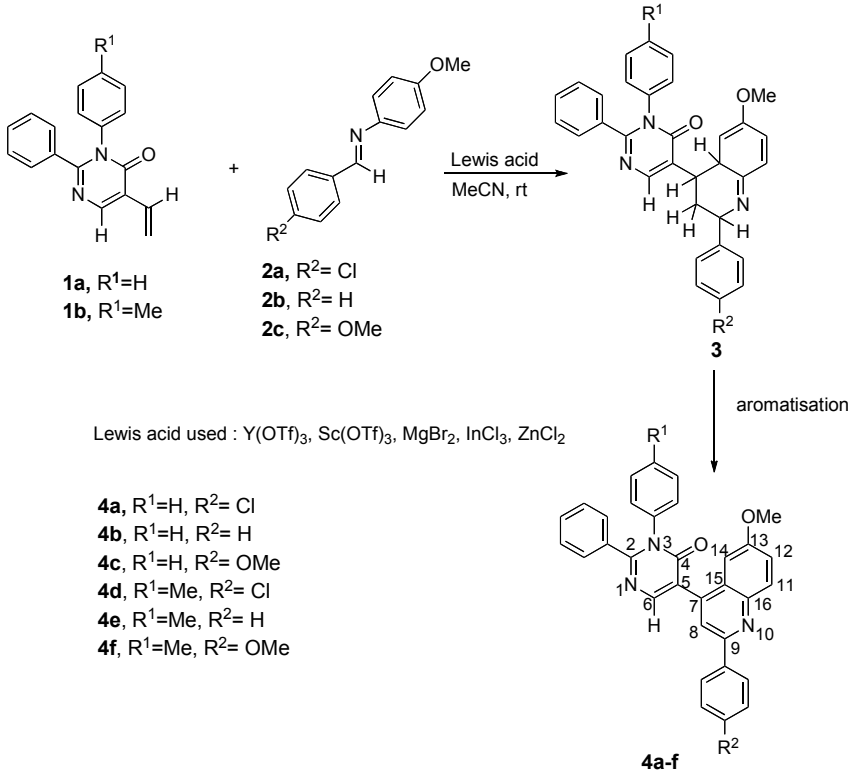
Figure 1 Dienic/dienophilic behaviour of conjugated hindered alkenes and *N*-aryl-imines towards IDA reaction

RESULTS AND DISCUSSION

Different Lewis acids *viz.* magnesium(II) bromide, zinc(II) chloride, indium(III) chloride, yttrium triflate and scandium triflate were selected for examination of their effects on the chemo- and regioselectivities of the IDA reactions of **1** with *N*-arylimines **2**.

The reactions of **1a-b** with *N*-arylimines **2a-c** in the presence of yttrium triflate as Lewis acid catalyst resulted in the formation of 5-quinoline substituted pyrimidinone derivatives **4a-f** in good yields (Table 1, Entries 1-3). The reactions in the presence of scandium triflate, magnesium(II) bromide, zinc (II) chloride and indium(III) chloride (Table 1, Entries 4-15), were found to be slower and required longer reaction periods for their completion with the formation of **4a-f** in moderate to good.

The products were characterized on the basis of analytical and spectral data, as described in the experimental section while the salient features are mentioned here. The compound **4a,** for example, showed a $[M+1]^+$ peak at m/z 516 in its mass spectrum. Its IR spectrum showed a strong absorption at 1670 cm^{-1} due to the carbonyl group of the pyrimidinone ring. Its ^1H NMR (300 MHz) spectrum showed singlets at δ 7.97 and δ 8.55 assigned to H_6 of the pyrimidinone ring and H_8 of the quinoline ring, respectively. The formation of pyrimidinones **4** in these reactions presumably involves regioselective IDA reactions of vinyl pyrimidinones **1** with *N*-arylimines **2** participating as 2-azadienes leading to the initial formation and subsequent aromatization of cycloadducts **3.**[8]



1a, R^1=H
1b, R^1=Me

2a, R^2= Cl
2b, R^2= H
2c, R^2= OMe

3

4a, R^1=H, R^2= Cl
4b, R^1=H, R^2= H
4c, R^1=H, R^2= OMe
4d, R^1=Me, R^2= Cl
4e, R^1=Me, R^2= H
4f, R^1=Me, R^2= OMe

4a-f

Scheme 1

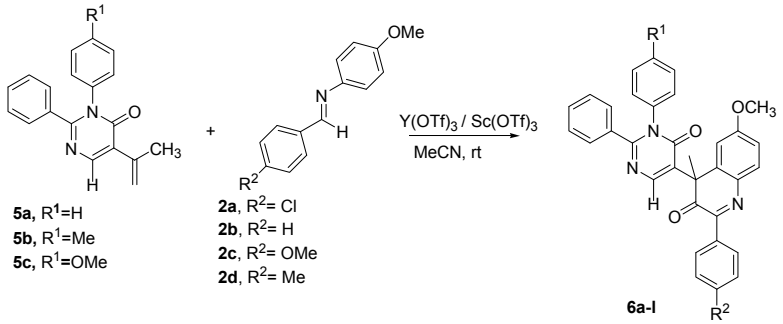
Table 1. Reactions of 5-vinyl pyrimidinones **1a-b** with *N*-aryl imines **2a-d**

Entry	Pyrimidinone	Imines	Metal salt	Time (h)	Product	Yield (%)[a]
1	**1a/b**	**2a**	$Y(OTf)_3$	14/12	**4a/4d**	85/79
2	**1a/b**	**2b**	$Y(OTf)_3$	15/12	**4b/4e**	82/86
3	**1a/b**	**2c**	$Y(OTf)_3$	13/14	**4c/4f**	75/75
4	**1a/b**	**2a**	$Sc(OTf)_3$	17/14	**4a/4d**	77/67
5	**1a/b**	**2b**	$Sc(OTf)_3$	16/17	**4b/4e**	74/75
6	**1a/b**	**2c**	$Sc(OTf)_3$	16/15	**4c/4f**	72/68
7	**1a/b**	**2a**	$MgBr_2$	24/20	**4a/4d**	79/78
8	**1a/b**	**2b**	$MgBr_2$	24/26	**4b/4e**	76/72
9	**1a/b**	**2c**	$MgBr_2$	25/25	**4c/4f**	70/76
10	**1a/b**	**2a**	$ZnCl_2$	30/32	**4a/4d**	69/70
11	**1a/b**	**2b**	$ZnCl_2$	28/30	**4b/4e**	67/68
12	**1a/b**	**2c**	$ZnCl_2$	30/30	**4c/4f**	66/67
13	**1a/b**	**2a**	$InCl_3$	30/32	**4a/4d**	64/73
14	**1a/b**	**2b**	$InCl_3$	29/30	**4b/4e**	72/66
15	**1a/b**	**2c**	$InCl_3$	28/29	**4c/4f**	68/64

[a] The reported yields pertain to crude products prior to recrystallization

In order to extend the scope of such studies to the IDA reactions of sterically more hindered alkenes, we have examined the reactions of 5-isopropenyl pyrimidinones **5** with *N*-arylimines **2** in the presence of various (lanthanide and non-lanthanide) Lewis acid catalysts. Interestingly, these reactions in the presence of 10 mol % of $Y(OTf)_3$ and $Sc(OTf)_3$ in acetonitrile resulted in regio- and chemoselective formation of

6-oxo-1,6-dihydropyrimidin-5-yl-4*H*-quinolin-3-one derivatives **6** (Scheme2; Table 2; Entries 1-8). The yields of the oxidized cycloadducts were found to be higher in presence of $Y(OTf)_3$ (Entries 1-4) as compared to $Sc(OTf)_3$ (Table 2, entry 5-7).

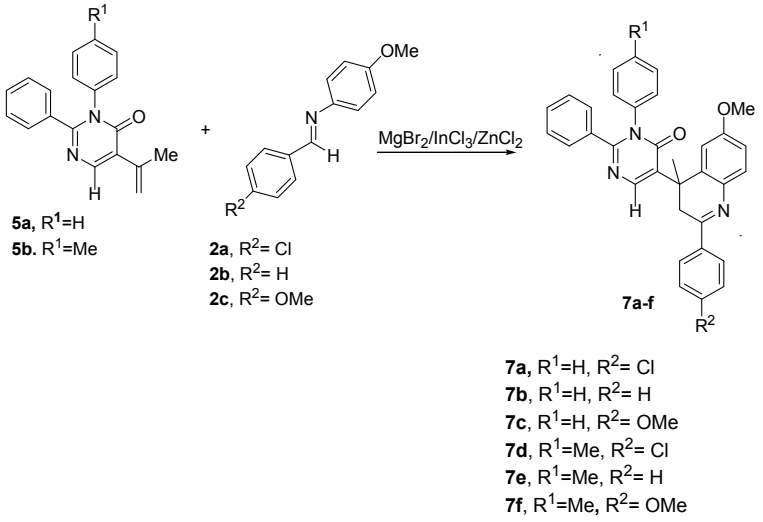


Scheme 2

The structure **6** was assigned to the products with the help of analytical data and spectral evidences. The pyrimidinone **6a,** for example, exhibited a molecular ion peak at m/z 546 in its mass spectrum. Its IR spectrum showed the pyrimidinone and pyridone carbonyl absorptions at 1666 $cm^{-1}$and 1687 cm^{-1} respectively. Its ^1H NMR spectrum showed the absence of methylene protons, the presence of a three proton singlet at δ 1.73 due to the methyl protons of the quinoline-3-one ring and a characteristic singlet at δ 8.34 for the olefinic proton of the pyrimidinone ring. Its ^{13}C NMR spectrum showed pyrimidinone and quinolinone carbonyls at δ 160.5 and 193.7 ppm, respectively. The assigned structure **6a** was unambiguously established with the help of X-ray crystallographic studies.[6a]

The precise mechanism for the oxidation of methylene to carbonyl observed in these reactions could not be ascertained, however, it may involve a mechanism similar to the one observed in $Yb(OTf)_3$.[9] Alternatively, it may take place *via* a charge transfer complex followed by the formation of radical cation as observed in $Ce(OTf)_3$.[10]

However, the reactions of pyrimidinones **5a-b** with **2a-c** in the presence of non-triflate Lewis acid catalysts, *viz* $MgBr_2$, $InCl_3$, $ZnCl_2$ and resulted in the formation of previously unreported 3, 4-dihydroquinolin-4-ylpyrimidin-4-one derivatives **7a-f** in good yields (Table 2; Entries 9-20). The use of magnesium (II) bromide as catalyst resulted in better yields of adducts while moderate yield of adducts **7** were obtained when indium (III) chloride and zinc (II) chloride were used as catalysts.



Scheme 3

Table 2. Reactions of 5- vinyl pyrimidinones **5a-b** with **2a-c**

Entry	Pyrimidinone	Imines	Metal salts	Time	Product	Yields[a]
1	**5a/b/c**	**2a**	$Y(OTf)_3$	12/14/15	**6a/6e/6i**	82/79/74
2	**5a/b/c**	**2b**	$Y(OTf)_3$	12/13/13	**6b/6f/6j**	88/85/79
3	**5a/b/c**	**2c**	$Y(OTf)_3$	14/12/12	**6c/6g/6k**	79/75/72
4	**5a/b/c**	**2d**	$Y(OTf)_3$	13/12/12	**6d/6h/6l**	75/85/83
5	**5a/b/c**	**2a**	$Sc(OTf)_3$	14/15/17	**6a/6e/6i**	73/81/74
6	**5a/b/c**	**2b**	$Sc(OTf)_3$	16/17/16	**6b/6f/6j**	79/84/80
7	**5a/b/c**	**2c**	$Sc(OTf)_3$	17/18/17	**6c/6g/6k**	76/78/75
8	**5a/b/c**	**2d**	$Sc(OTf)_3$	17/18/18	**6d/6h/6l**	75/76/73
9	**5a/b**	**2a**	$MgBr_2$	26/24	**7a/7d**	67/71
10	**5a/b**	**2b**	$MgBr_2$	26/25	**7b/7e**	65/78
11	**5a/b**	**2c**	$MgBr_2$	24/24	**7c/7f**	68/70
13	**5a/b**	**2a**	$ZnCl_2$	29/30	**7a/7d**	64/59
14	**5a/b**	**2b**	$ZnCl_2$	30/32	**7b/7e**	57/51
15	**5a/b**	**2c**	$ZnCl_2$	28/28	**7c/7f**	59/58
17	**5a/b**	**2a**	$InCl_3$	32/30	**7a/7d**	62/66
18	**5a/b**	**2b**	$InCl_3$	36/32	**7b/7e**	72/78
19	**5a/b**	**2c**	$InCl_3$	30/32	**7c/7f**	71/65

[a] The reported yields pertain to crude products prior to re-crystallization

Thus, the oxidation of methylene to carbonyl, observed in reactions of **5a-c** with **2a-d** in the presence of $Y(OTf)_3$/ $Sc(OTf)_3$ as catalysts, was not observed when these reactions were performed in the presence of non-triflate LA catalysts. The structure **7** was also assigned on the basis of analytical data and spectral evidences. The ^{1}H NMR spectrum of **7a** exhibited characteristic doublets at δ 2.35 (J=16.5Hz) and δ 4.35 (J=16.5Hz) assigned to the methylene protons of the quinoline ring. The methylene carbon of the quinoline ring appeared at δ 38.4 in its ^{13}C NMR. The oxidation of methylene to carbonyl in the presence of $Y(OTf)_3$/ $Sc(OTf)_3$ catalysts is also supported by the independent transformation of **7** to **6** in the

presence of 10 mol% of $Y(OTf)_3$ / $Sc(OTf)_3$ in acetonitrile at room temperature.

CONCLUSION

In conclusion, this manuscript describes the regio- and catalyst selective Imino Diels–Alder reactions of sterically hindered and geminally di-substituted alkenes *viz.* 5-vinyl and isopropenyl-pyrimidinones with *N*-arylimines. The reactions resulted in the synthesis of quinoline-tethered pyrimidinone derivatives in case of vinyl-pyrimidinones **1a-b** using triflate as well as non-triflate Lewis acid catalysts, since aromatization of initial IDA adducts is a favored process. However, in case of isopropenyl-pyrimidinones **5a-c**, where aromatization of IDA adducts is not possible due to the presence of the methyl group, the reactions accompanied an unprecedented oxidation of methylene to carbonyl in the presence of $Y(OTf)_3$/ $Sc(OTf)_3$ leading to the formation of quinolone substituted pyrimidinone derivatives.

EXPERIMENTAL

GENERAL REMARKS

Melting points were determined by open capillary using a Veego Precision Digital Melting Point apparatus (MP-D) and are uncorrected. IR spectra were recorded on a Shimadzu D-8001 spectrophotometer. ^{1}H NMR spectra were recorded in deuteriochloroform with a Joel (300 MHz) spectrometers using TMS as internal standard. Chemical shift values are expressed as ppm downfield from TMS and *J* values are in Hz. Splitting patterns are indicated as s: singlet, d: doublet, t: triplet, m: multiplet, q: quartet, br: broad peak and brs: broad singlet. ^{13}C NMR spectra were also recorded on a Joel 300 (75.0 MHz) spectrometers in deuteriochloroform using TMS as internal standard. Mass spectra were recorded on a Shimadzu GCMS-QP-2000 mass spectrometer. Elemental analyses were performed on a Heraus CHN-O-Rapid Elemental Analyzer. Column chromatography was performed on a silica gel (60–120 mesh).

GENERAL PROCEDURE

5-Vinyl/isopropenyl pyrimidinones were prepared by the reported methods.[11] The typical procedure for IDA reactions involved the addition of 10 mol % of Lewis acid to a well stirred solution of *N*-arylimine (1 mmol) in dry acetonitrile (10 mL) at rt. The solution was allowed to stir for 5-min. followed by the addition of vinyl/isopropenyl pyrimidinones (1 mmol). The progress of the reaction was monitored by tlc using pyrimidinone as the limiting reactant. On completion, the reaction mixture was quenched with a water/MeOH mixture, extracted with CH_2Cl_2 and concentrated under reduced pressure. Column

chromatography of the crude reaction mixture using a mixture of EtOAc: hexane (1:4) as an eluent resulted in the products which were recrystallized using a mixture of hexane: DCM (5:1).

5-[2-(4-Chlorophenyl)-6-methoxy-quinolin-4-yl]-2,3-diphenyl-3*H*-pyrimidin-4-one **4a.**
Yellow solid; mp 165-166 ^{0}C ; IR (KBr) ν_{max} 1670 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 3.88 (s, 3H, OCH_3), 7.06- 7.50(m, 14H, ArH), 7.97(s, 1H, H^8), 8.12 (m, 3H, H^{11}, H^{12}, H^{14}), 8.55(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 55.7 (-OCH_3), 101.8, 114.2, 122.0, 124.4, 126.3, 127.2, 127.9, 128.4, 128.8, 129.0, 129.2, 129.7, 131.4, 134.5, 134.8, 137.5, 138.6, 144.4, 150.2, 153.5, 155.4, 155.6, 158.2, 161.2.; MS m/z $[M+1]^+$: 516; Anal. Calcd for $C_{32}H_{22}ClN_3O_2$: C, 74.49; H, 4.30; N, 8.14. Found: C, 74.54; H, 4.82; N, 8.02.

5-(6-Methoxy-2-phenylquinolin-4-yl)-2,3-diphenyl-3*H*-pyrimidin-4-one **4b.**
Yellow solid; mp 171-172 ^{0}C; IR (KBr) ν_{max} 1667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 3.81 (s, 3H, OCH_3), 7.04- 7.55(m, 15H, ArH), 7.98(s, 1H, H^8), 8.10 (m, 3H, H^{11}, H^{12}, H^{14}), 8.52(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 56.2 (-OCH_3), 101.1, 113.9, 121.8, 123.8, 126.5, 127.1, 127.5, 128.3, 128.7, 129.2, 129.4, 129.8, 131.2, 134.4, 134.7, 137.6, 138.3, 144.5, 149.9, 153.6, 155.6, 155.7, 158.3, 161.2.; MS m/z $[M+1]^+$: 482; Anal. Calcd for $C_{32}H_{23}N_3O_2$: C, 79.81; H, 4.81; N, 8.73. Found: C, 79.74; H, 4.72; N, 8.65.

5-[6-Methoxy-2-(4-methoxyphenyl)-quinolin-4-yl]-2, 3-diphenyl-3*H*-pyrimidin-4-one **4c.**
Yellow solid; mp 159-160 ^{0}C; IR (KBr) ν_{max} 1672 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 3.79 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 7.10- 7.46(m, 14H, ArH), 7.98(s, 1H, H^8), 8.10 (m, 3H, H^{11}, H^{12}, H^{14}), 8.52(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 56.0(-OCH_3), 56.2 (-OCH_3), 100.9, 114.0, 121.6, 123.5, 126.7, 126.8, 127.6, 128.4, 128.6, 129.3, 129.5, 129.9, 130.9, 133.8, 134.2, 137.2, 138.0, 144.1, 149.7, 153.5, 155.4, 155.8, 158.2, 161.3.; MS m/z $[M+1]^+$: 512; Anal. Calcd for $C_{33}H_{25}N_3O_3$: C, 77.48; H, 4.93; N, 8.21. Found: C, 77.35; H, 4.82; N, 8.05.

5-(6-Methoxy-2-phenylquinolin-4-yl)-2-phenyl-3-p-tolyl-3*H*-pyrimidin-4-one **4d.**
Yellow solid; mp 162-163 ^{0}C; IR (KBr) ν_{max} 1665 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 2.28 (s, 3H, CH_3), 3.74(s, 3H, OCH_3), 7.12-7.48(m, 14H, ArH), 8.05 (s, 1H, H^8), 8.09 (m, 3H, H^{11}, H^{12}, H^{14}), 8.35(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 16.7(CH_3), 56.2(-OCH_3), 101.2, 114.1, 121.9, 123.8, 125.8, 126.3, 127.3, 128.0, 128.7, 129.2, 129.6, 130.3, 131.3, 134.1, 134.6, 137.5, 138.8, 144.2, 150.5, 153.5, 155.6, 155.7, 158.5, 161.0.; MS m/z $[M+1]^+$: 496; Anal. Calcd for $C_{33}H_{25}N_3O_2$: C, 79.98; H, 5.08; N, 8.48. Found: C, 79.73; H, 5.13; N, 8.52.

5-[2-(4-Chlorophenyl)-6-methoxy-quinolin-4-yl]-2-phenyl-3-p-tolyl-3*H*-pyrimidin-4-one **4e.**
Yellow solid; mp 176-177 ^{0}C; IR (KBr) ν_{max} 1668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 2.31 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 7.02- 7.52(m, 13H, ArH), 7.94(s, 1H, H^8), 8.13 (m, 3H, H^{11}, H^{12}, H^{14}), 8.55(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : δ 19.6 (-CH_3), 55.9 (-OCH_3), 101.6, 114.4, 122.2, 124.5, 126.6, 127.4, 127.9, 128.5, 128.7, 129.0, 129.4, 129.8, 131.5, 134.6, 134.9, 137.5, 138.6, 143.9, 153.5, 155.5, 155.7, 158.2, 161.0.; MS m/z $[M+1]^+$: 530; Anal. Calcd for $C_{33}H_{24}ClN_3O_2$: C, 74.78 ; H, 4.56; N, 7.93. Found: C, 74.80; H, 4.62; N, 7.85.

5-[6-Methoxy-2-(4-methoxyphenyl)-quinolin-4-yl]-2-phenyl-3-p-tolyl-3*H*-pyrimidin-4-one **4f.**
Yellow solid; mp 178-179 ^{0}C; IR (KBr) ν_{max} 1666 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 2.32 (s, 3H, CH_3), 3.88 (s, 6H, OCH_3), 7.09- 7.59(m, 13H, ArH), 7.98(s, 1H, H^8), 8.15 (m, 3H, H^{11}, H^{12}, H^{14}), 8.50(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : δ 19.9 (-CH_3), 55.8 (-OCH_3), 56.0 (-OCH_3), 100.6, 113.9, 122.5, 123.9, 126.4, 127.7, 128.1, 128.7, 128.9, 129.2, 129.4, 129.9, 131.4, 134.3, 134.8, 137.3, 138.3, 143.7, 153.6, 155.3, 155.9, 158.4, 160.8; MS m/z $[M+1]^+$: 526; Anal. Calcd for $C_{34}H_{27}N_3O_3$: C, 77.48 ; H, 5.18; N, 7.99. Found: C, 77.80; H, 5.22; N, 7.86.

2-(4-Chlorophenyl)-6-methoxy-4-methyl-4-(6-oxo-1,2-diphenyl-1,6-dihydropyrimidin-5-yl)-4*H*-quinolin-3-one **6a.**
Yellow solid; mp 146-147 ^{0}C; IR (KBr) ν_{max} 1666, 1687 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) : δ 1.73(s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 6.65-7.99 (m, 17H, ArH), 8.34(s,1H olefinic proton), ^{13}C NMR (150 MHz, $CDCl_3$) : 24.8(-CH_3), 51.1(C-7, quinolin-3-one ring), 55.5(-OCH_3), 111.4, 112.7, 123.6, 127.9, 128.0, 128.4, 128.6, 128.65, 128.8, 129.0, 129.2, 129.8, 129.9, 132.7, 134.3, 134.9, 135.3, 136.6, 138.8, 149.4, 154.1, 159.3, 160.3, 160.5 (C=O, pyrimidinone ring), 193.7 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 546; Anal. Calcd for $C_{33}H_{24}ClN_3O_3$: C, 72.59; H, 4.43; N, 7.70. Found: C, 72.71; H, 4.54; N, 7.79.

6-Methoxy-4-methyl-4-(6-oxo-1,2-diphenyl-1,6-dihydropyrimidin-5-yl)-2-phenyl-4*H*-quinolin-3-one **6b.**
Yellow solid; mp 149-150 ^{0}C; IR (KBr) ν_{max} 1665, 1689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.73(s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 6.69-7.98 (m, 18H, ArH), 8.35(s, 1H olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 24.5(-CH_3), 51.2(C-7, quinolin-3-one ring), 55.6(-OCH_3), 111.2, 112.6, 123.5, 127.9, 128.1, 128.3, 128.5, 128.6, 128.9, 129.0, 129.3, 129.7, 129.8, 132.6, 134.4, 134.8, 135.4, 136.6, 138.8, 149.5, 154.2, 159.1, 160.2, 160.5 (C=O, pyrimidinone ring), 193.5 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 512; Anal. Calcd for $C_{33}H_{25}N_3O_3$: C, 77.48; H, 4.93; N, 8.21. Found: C, 77.66; H, 4.84; N, 8.34.

6-Methoxy-2-(4-methoxyphenyl)-4-methyl-4-(6-oxo-1,2-diphenyl-1,6-dihydropyrimidin-5-yl)-4*H*-quinolin-3-one **6c.**

Yellow solid; mp 155-156 ^{0}C; IR (KBr) ν_{max} 1665, 1688 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.72(s, 3H, CH_3), 3.86(s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.66-7.94 (m, 17H, ArH), 8.34(s, 1H olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 24.4(-CH_3), 51.0(C-7, quinolin-3-one ring), 55.5(-OCH_3), 55.6(-OCH_3), 111.3, 112.6, 123.6, 127.8, 128.1, 128.2, 128.4, 128.6, 128.8, 129.1, 129.4, 129.7, 129.9, 132.5, 134.4, 134.7, 135.6, 136.5, 138.9, 149.4, 154.0, 159.2, 160.3, 160.4 (C=O, pyrimidinone ring), 193.6 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 542; Anal. Calcd for $C_{34}H_{27}N_3O_4$: C, 75.40; H, 5.02; N, 7.76. Found: C, 75.54; H, 5.55; N, 7.45.

6-Methoxy-4-methyl-4-(6-oxo-1,2-diphenyl-1,6-dihydropyrimidin-5-yl)-2-*p*-tolyl-4*H*-quinolin-3-one **6d.**

Yellow solid; mp 132-133 ^{0}C; IR (KBr) ν_{max} 1666, 1689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.73(s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.86(s, 3H, OCH_3), 6.65-7.95 (m, 17H, ArH), 8.31(olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 20.4(-CH_3), 24.4(-CH_3), 51.2(C-7, quinolin-3-one ring), 55.5(-OCH_3), 111.1, 112.5, 123.4, 127.7, 128.0, 128.1, 128.4, 128.5, 128.7, 129.2, 129.5, 129.6, 129.8, 132.5, 134.5, 134.6, 135.7, 136.6, 138.8, 149.6, 154.1, 159.1, 160.2, 160.4 (C=O, pyrimidinone ring), 193.5 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 526; Anal. Calcd for $C_{34}H_{27}N_3O_3$: C, 77.70; H, 5.18; N, 7.99. Found: C, 77.94; H, 5.35; N, 7.88.

2-(4-Chlorophenyl)-6-methoxy-4-methyl-4-(6-oxo-2-phenyl-1-*p*-tolyl-1,6-dihydropyrimidin-5-yl)-4*H*-quinolin-3-one **6e.**

Yellow solid; mp 143-144 ^{0}C; IR (KBr) ν_{max} 1665, 1687 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.72(s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.89(s, 3H, OCH_3), 6.68-7.99 (m, 17H, ArH), 8.34(s, 1H olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 19.3(-CH_3), 24.4(-CH_3), 51.0(C-7, quinolin-3-one ring), 55.7(-OCH_3), 111.1, 112.3, 123.5, 127.7, 128.0, 128.2, 128.3, 128.5, 128.6, 129.5, 129.6, 129.8, 129.9, 132.2, 134.3, 134.5, 135.7, 136.8, 138.6, 149.4, 154.3, 159.1, 160.2, 160.5 (C=O, pyrimidinone ring), 193.6 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 560; Anal. Calcd for $C_{34}H_{26}ClN_3O_3$: C, 72.92; H, 4.68; N, 7.50. Found: C, 72.98; H, 4.55; N, 7.76.

6-Methoxy-4-methyl-4-(6-oxo-2-phenyl-1-*p*-tolyl-1,6-dihydropyrimidin-5-yl)-2-phenyl-4*H*-quinolin-3-one **6f.**

Yellow solid; mp 140-141 ^{0}C; IR (KBr) ν_{max} 1667, 1688 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.72(s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.86(s, 3H, OCH_3), 6.66-7.97 (m, 17H, ArH), 8.33(s, 1H olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 19.5(-CH_3), 24.3(-CH_3), 51.1(C-7, quinolin-3-one ring), 55.6(-OCH_3), 111.2,

112.5, 123.3, 127.6, 128.1, 128.3, 128.4, 128.6, 128.7, 129.4, 129.5, 129.7, 129.8, 132.6, 134.4, 134.5, 135.8, 136.7, 138.7, 149.5, 154.2, 159.0, 160.1, 160.5 (C=O, pyrimidinone ring), 193.7 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 526; Anal. Calcd for $C_{34}H_{27}N_3O_3$: C, 77.70; H, 5.18; N, 7.99. Found: C, 77.88; H, 5.12; N, 7.92.

6-Methoxy-2-(4-methoxy-phenyl)-4-methyl-4-(6-oxo-2-phenyl-1-*p*-tolyl-1,6-dihydropyrimidin-5-yl)-4*H*-quinolin-3-one **6g**.

Yellow solid; mp 138-139 ^{0}C ; IR (KBr) ν_{max} 1666, 1689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.73(s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.86(s, 3H, OCH_3), 3.87(s, 3H, OCH_3), 6.67-7.95 (m, 17H, ArH), 8.32(olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 19.5(-CH_3), 24.5(-CH_3), 51.2(C-7, quinolin-3-one ring), 55.5(-OCH_3), 55.6(-OCH_3), 111.3, 112.5, 123.5, 127.8, 128.2, 128.3, 128.4, 128.5, 128.7, 129.4, 129.7, 129.8, 129.9, 132.1, 134.4, 134.6, 135.7, 136.7, 138.5, 149.5, 154.4, 159.2, 160.1, 160.4 (C=O, pyrimidinone ring), 193.5 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 556; Anal. Calcd for $C_{35}H_{29}N_3O_4$: C, 75.66; H, 5.26; N, 7.56. Found: C, 75.77; H, 5.40; N, 7.42.

6-Methoxy-4-methyl-4-(6-oxo-2-phenyl-1-*p*-tolyl-1,6-dihydropyrimidin-5-yl)-2-*p*-tolyl-4*H*-quinolin-3-one **6h.**

Yellow solid; m.p. 134-135 ^{0}C; IR (KBr) ν_{max} 1665, 1688 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.73(s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.87(s, 3H, OCH_3), 6.66-7.98 (m, 17H, ArH), 8.34(s, 1H olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 19.5(-CH_3), 19.8(CH_3), 24.5(-CH_3), 51.1(C-7, quinolin-3-one ring), 55.7(-OCH_3), 111.1, 112.2, 123.4, 127.6, 128.3, 128.4, 128.6, 128.7, 128.9, 129.5, 129.7, 129.8, 129.9, 132.3, 134.5, 134.8, 135.7, 136.6, 138.8, 149.5, 154.5, 159.4, 160.1, 160.5 (C=O, pyrimidinone ring), 193.7 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 540; Anal. Calcd for $C_{35}H_{29}N_3O_3$: C, 77.90; H, 5.42; N, 7.79. Found: C, 77.84; H, 5.40; N, 7.83.

2-(4-Chlorophenyl)-6-methoxy-4-[1-(4-methoxy-phenyl)-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl]-4-methyl-4*H*-quinolin-3-one **6i**.

Yellow solid; mp 136-137 ^{0}C; IR (KBr) ν_{max} 1667, 1688 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.71(s, 3H, CH_3), 3.86(s, 3H, OCH_3), 3.88(s, 3H, OCH_3), 6.64-7.95 (m, 17H, ArH), 8.32(s, 1H olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 24.8(-CH_3), 51.2(C-7, quinolin-3-one ring), 55.6(-OCH_3), 55.7(-OCH_3), 111.2, 112.4, 123.6, 127.6, 128.1, 128.2, 128.5, 128.7, 128.8, 129.5, 129.6, 129.7, 129.9, 132.4, 134.6, 134.5, 135.6, 136.6, 138.8, 149.5, 154.5, 159.2, 160.1, 160.5 (C=O, pyrimidinone ring), 193.5 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 576; Anal. Calcd for $C_{34}H_{26}ClN_3O_4$: C, 70.89; H, 4.55; N, 7.29. Found: C, 70.81; H, 4.93; N, 7.38.

6-Methoxy-4-[1-(4-methoxyphenyl)-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl]-4-methyl-2-phenyl-4*H*-quinolin-3-one **6j.**

Yellow solid; mp 152-153 ^{0}C; IR (KBr) ν_{max} 1665, 1687 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.73(s, 3H, CH_3), 3.86(s, 3H, OCH_3), 3.87(s, 3H, OCH_3), 6.67-7.99 (m, 17H, ArH), 8.31(s, 1H olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 24.6(-CH_3), 51.3(C-7, quinolin-3-one ring), 55.5(-OCH_3), 55.7(-OCH_3), 111.3, 112.3, 123.5, 127.7, 128.2, 128.4, 128.7, 128.8, 128.9, 129.6, 129.7, 129.8, 129.9, 132.4, 134.5, 134.6, 135.8, 136.7, 138.9, 149.3, 154.4, 159.3, 160.0, 160.3 (C=O, pyrimidinone ring), 193.6 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 542; Anal. Calcd for $C_{34}H_{27}N_3O_4$: C, 75.40; H, 5.02; N, 7.76. Found: C, 75.54; H, 4.99; N, 7.81.

6-Methoxy-2-(4-methoxyphenyl)-4-[1-(4-methoxy-phenyl)-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl]-4-methyl-4*H*-quinolin-3-one **6k**.

Yellow solid; mp 128-129 ^{0}C; IR (KBr) ν_{max} 1665, 1689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.73(s, 3H, CH_3), 3.87(s, 6H, OCH_3), 3.88(s, 3H, OCH_3), 6.67-7.98 (m, 17H, ArH), 8.34(s, 1H olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 24.7(-CH_3), 51.2(C-7, quinolin-3-one ring), 55.6(-OCH_3), 55.6(-OCH_3), 55.7(-OCH_3), 111.4, 112.5, 123.4, 127.6, 128.3, 128.4, 128.5, 128.6, 128.7, 129.7, 129.8, 129.9, 130.1, 132.2, 134.4, 134.5, 135.6, 136.5, 138.7, 149.4, 154.4, 159.1, 160.1, 160.4 (C=O, pyrimidinone ring), 193.6 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 572; Anal. Calcd for $C_{35}H_{29}N_3O_5$: C, 73.54; H, 5.11; N, 7.35. Found: C, 73.78; H, 5.25; N, 7.32.

6-Methoxy-4-[1-(4-methoxyphenyl)-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl]-4-methyl-2-*p*-tolyl-4*H*-quinolin-3-one **6l**.

Yellow solid; mp 130-131 ^{0}C; IR (KBr) ν_{max} 1666, 1689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.71(s, 3H, CH_3), 3.86(s, 3H, OCH_3), 3.88(s, 3H, OCH_3), 6.65-7.96 (m, 17H, ArH), 8.35(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 24.8(-CH_3), 51.1(C-7, quinolin-3-one ring), 55.5(-OCH_3), 55.6(-OCH_3), 111.3, 112.4, 123.5, 127.7, 128.3, 128.5, 128.6, 128.7, 128.8, 129.7, 129.8, 129.9, 130.2, 132.3, 134.5, 134.6, 135.6, 136.6, 138.8, 149.5, 154.5, 159.2, 160.3, 160.5 (C=O, pyrimidinone ring), 193.5 (C=O, quinolin-3-one ring): MS m/z $[M+1]^+$: 556; Anal. Calcd for $C_{35}H_{29}N_3O_4$: C, 75.66; H, 5.26; N, 7.56. Found: C, 75.75; H, 5.32; N, 7.63.

5-[2-(4-Chlorophenyl)-6-methoxy-4-methyl-3,4-dihydroquinolin-4-yl]-2,3-diphenyl-3*H*-pyrimidin-4-one **7a**.

Yellow solid; mp 179-180 ^{0}C; IR (KBr) ν_{max} 1668 cm^{-1}; ^{1}HN MR (300 MHz, $CDCl_3$) : δ 1.87 (s, 3H, CH_3), 2.35 (d, 1H, J =16.5 Hz), 3.88 (s, 3H, OCH_3), 4.35(d, 1H, J = 16.5 Hz), 7.08-7.51(m, 17H, ArH),

7.95(s,1H, olefinic proton), ^{13}CNMR (75MHz, $CDCl_3$) :21.1(-CH_3), 23.6(C-7), 38.3(-CH_2-dihydroquinoline ring), 56.7(-OCH_3), 111.4, 112.0, 113.4, 121.2, 124.9, 127.3, 127.8, 128.1, 128.5, 128.6, 128.9, 129.5, 129.7, 130.6, 132.2, 132.9,134.4, 136.1, 150.4, 159.0, 161.2; MS m/z $[M+1]^+$: 532; Anal. Calcd for $C_{33}H_{26}ClN_3O_2$: C, 74.50; H, 4.93; N, 7.90. Found: C, 74.84; H, 4.82; N, 7.99.

5-(6-Methoxy-4-methyl-2-phenyl-3,4-dihydro-quinolin-4-yl)-2,3-diphenyl-3*H*-pyrimidin-4-one **7b**.
Yellow solid; mp 185-186 ^{0}C; IR (KBr) ν_{max} 1667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.87 (s, 3H, CH_3), 2.37 (d, 1H, *J* =16.5 Hz), 3.89 (s, 3H, OCH_3), 4.37(d, 1H, *J* = 16.5 Hz), 7.02-7.55(m, 18H, ArH), 7.99(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 21.4(-CH_3), 23.6(C-7), 38.5(-CH_2-dihydroquinoline ring), 56.6(-OCH_3), 111.6, 112.1, 113.3, 121.4, 124.8, 127.5, 127.8, 128.2, 128.5, 128.6, 128.8, 129.6, 129.9, 130.5, 132.3, 132.8, 134.8, 136.3, 150.1, 159.2, 161.1; MS m/z $[M+1]^+$: 498; Anal. Calcd for $C_{33}H_{27}N_3O_2$: C, 79.66; H, 5.47; N, 8.44. Found: C, 79.82; H, 5.55; N, 8.49.

5-[6-Methoxy-2-(4-methoxyphenyl)-4-methyl-3,4-dihydroquinolin-4-yl]-2,3-diphenyl-3*H*-pyrimidin-4-one **7c**.
Yellow solid; mp 188-189 ^{0}C; IR (KBr) ν_{max} 1668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.88 (s, 3H, CH_3), 2.34 (d, 1H, *J* =16.4 Hz), 3.84 (s, 6H, OCH_3), 4.36(d, 1H, *J* = 16.4 Hz), 7.03-7.53(m, 17H, ArH), 7.98(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 21.4(-CH_3), 23.6(C-7), 38.5(-CH_2-dihydroquinoline ring), 56.5(-OCH_3), 56.6(-OCH_3), 111.3, 112.4, 113.7, 121.3, 124.7, 127.6, 127.7, 128.3, 128.4, 128.5, 128.8, 129.2, 129.7, 130.4, 132.4, 132.7, 134.5, 136.4, 150.0, 159.4, 161.3; MS m/z $[M+1]^+$: 528; Anal. Calcd for $C_{34}H_{29}N_3O_3$: C, 77.40; H, 5.54; N, 7.90. Found: C, 77.50; H, 5.45; N, 7.85.

5-[2-(4-Chlorophenyl)-6-methoxy-4-methyl-3,4-dihydroquinolin-4-yl]-2-phenyl-3-p-tolyl-3*H*-pyrimidin-4-one **7d.**
Yellow solid; mp 199-200 ^{0}C; IR (KBr) ν_{max} 1668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.89(s, 3H, CH_3), 2.33(s, 3H, CH_3), 2.36 (d, 1H, *J* =16.5 Hz), 3.89 (s, 3H, OCH_3), 4.34(d, 1H, *J* = 16.5 Hz), 6.99-7.48(m, 16H, ArH), 8.01(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 19.8(-CH_3), 21.4(-CH_3), 23.5(C-7), 38.5(-CH_2-dihydroquinoline ring), 56.8(-OCH_3), 111.6, 112.5, 113.5, 121.4, 124.6, 127.5, 127.7, 128.3, 128.4, 128.6, 128.7, 129.1, 129.3, 130.2, 132.3, 132.8, 134.7, 136.7, 151.2, 159.2, 161.1; MS m/z $[M+1]^+$: 546; Anal. Calcd for $C_{34}H_{28}ClN_3O_2$: C, 74.78; H, 5.17; N, 6.49. Found: C, 74.70; H, 5.29; N, 6.44.

5-(6-Methoxy-4-methyl-2-phenyl-3,4-dihydro-quinolin-4-yl)-2-phenyl-3-p-tolyl-3*H*-pyrimidin-4-one **7e**.
Yellow solid; mp 190-191 ^{0}C; IR (KBr) ν_{max} 1665 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.87(s, 3H, CH_3),

2.31(s, 3H, CH_3), 2.35 (d, 1H, *J* =16.5 Hz), 3.85 (s, 3H, OCH_3), 4.36(d, 1H, *J* = 16.5 Hz), 7.02-7.50(m, 17H, ArH), 7.99(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 19.7(-CH_3), 21.2(-CH_3), 23.6(C-7), 38.3(-CH_2-dihydroquinoline ring), 56.6(-OCH_3), 110.9, 112.2, 113.3, 121.2, 124.5, 127.4, 127.6, 128.2, 128.4, 128.5, 128.6, 129.2, 129.4, 130.3, 132.2, 132.6, 134.7, 136.6, 151.1, 159.3, 160.8; MS m/z $[M+1]^+$: 512; Anal. Calcd for $C_{34}H_{29}N_3O_2$: C, 79.82; H, 5.71; N, 8.21. Found: C, 79.79; H, 5.89; N, 8.27.

5-[6-Methoxy-2-(4-methoxyphenyl)-4-methyl-3,4-dihydroquinolin-4-yl]-2-phenyl-3-p-tolyl-3*H*-pyrimidin-4-one **7f.**

Yellow solid; mp 195-196 ^{0}C; IR (KBr) ν_{max} 1667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 1.88(s, 3H, CH_3), 2.31(s, 3H, CH_3), 2.34 (d, 1H, *J* =16.4 Hz), 3.86 (s, 6H, OCH_3), 4.36(d, 1H, *J* = 16.4 Hz), 7.02-7.52(m, 16H, ArH), 8.01(s, 1H, olefinic proton), ^{13}C NMR (75 MHz, $CDCl_3$) : 19.9(-CH_3), 21.5(-CH_3), 23.7(C-7), 38.8(-CH_2-dihydroquinoline ring), 56.6(-OCH_3), 56.7(-OCH_3), 111.2, 112.5, 113.6, 121.7, 124.8, 127.5, 127.7, 128.2, 128.3, 128.5, 128.8, 129.2, 129.3, 130.3, 132.4, 132.7, 134.6, 136.8, 151.1, 159.5, 161.0; MS m/z $[M+1]^+$: 542; Anal. Calcd for $C_{35}H_{31}N_3O_3$: C, 77.61; H, 5.77; N, 7.66. Found: C, 77.77; H, 5.72; N, 7.47.

ACKNOWLEDGEMENTS

We are thankful to Professor Takao Saito, University of Science, Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan for providing 600 MHz NMR spectra. NMR facility of Department of Chemistry, GNDU, Amritsar funded by Department of Science and Technology, Govt. of India, is gratefully acknowledged.

REFERENCES

1. S. M. Weinreb, B. M. Trost, and I. Fleming, *Comprehensive Organic Synthesis*. Eds.; Pergamon: Oxford. 1991; *Vol.* **5**, 401–449; (b) D. L. Boger and S. M. Weinreb, *Hetero Diels–Alder Methodology in Organic Synthesis*. Academic: San Diego, 1987, Chapters 2 and 9.
2. (a) S. Kobayashi, H. Ishitani, and S. Nagayama, *Chem. Lett.,* 1995, **24**, 423; (b) H. Ishitani and S. Kobayashi, *Tetrahedron Lett.,* 1996, **37**, 7357; (c) S. Kobayashi, M. Araki, H. Ishitani, S. Nagayama, and I. Hachiya, *Synlett,* 1995, 233; (d) S. Kobayashi, H. Ishitani, and S. Nagayama, *Synthesis,* 1995, 1195.
3. (a) H. J. Roth and H. Fenner, *In Arzneistoffe, 3rd ed.; Deutscher Apotheker Verlag: Stuttgart.* 2000; pp. 51–114; (b) N. Yamada, S. Kadowaki, K. Takahashi, and K. Umezu, *Biochem. Pharmacol.,* 1992, **44**, 1211; (c) K. Faber, H. Stueckler, and T. Kappe, *J. Heterocycl. Chem*., 1984, **21**, 1177; (d) J. V. Johnson, B. S. Rauckmann, D. P. Baccanari, and B. Roth, *J. Med.*

Chem., 1989, **32**, 1942; (e) I. Nesterova, L. M. Alekseeva, A. L. Mndreeva, S. M. Golovira, and V. G. Granic, *Khim. Farm. Zh.,* 1995, **29**, 31; (f) K. J. Rajendra Prasad and M. Sekar, *J. Nat. Prod.,* 1998, **61**, 294; (g) S. E. Hagen, J. M. Domagala, C. L. Heifetz, J. P. Sanchez, and M. Solomon, *J. Med. Chem.,* 1990, **33**, 849; (h) M. Hadjeri, E.-L. Peiller, C. Beney, N. Deka, M. A. Lawson, C. Dumontet, and A. Boumendjel, *J. Med. Chem.,* 2004, **47***,* 4964; (i) S. C. Kuo, H. Lee, Z. Juang, J. P. Lin, Y. T. Wu, T. S. Cheng, J. J. Lednicer, D. Paull, K. D. Lin, C. M. Hamel, and E. Lee, *J. Med. Chem*., 1993, **36**, 1146.

4. (a) L. F. Tietze and G. Kettschau, *Top. Curr. Chem*., 1997, **189**, 1; (b) S. Kobayashi, *Eur. J. Org. Chem.,* 1999, 15; (c) M. Panunzio and P. Zarantonello, *Org. Process Res. Dev.,* 1988, **2**, 49; (d) D. Enders and O. Meyer, *Liebigs Ann. Chem.,* 1996, 1023; (e) H. Waldmann, *Organic Synthesis Highlights II.* H. Waldman, VCH: New York, NY, 1995; pp. 37-47; (f) H. Waldmann, *Synthesis,* 1994, 535; (g) H. Waldmann and M. Braun, *Gazz. Chim. Ital.,* 1991, **121**, 277; (h) H. Waldmann, *Synlett,* 1995, 133; (i) J. Barluenga, J. Joglar, J. F. Gonzalez, and S. Fustero, *Synlett,* 1990, 129; (j) D. T. Parker, *Organic Synthesis in Water;* P. A. Grieco, *Ed.;* Blackie Academic and Professional: London, 1998; **2**, pp. 47-81; (k) J. Barluenga and M. Tomas, *Adv. Heterocycl. Chem.,* 1993, **57**, 1; (l) P. Boonra, F. C. Oslen, and T. Oh, *Tetrahedron*, 2001, **54**, 6099.

5. For recent example on Imino DA reaction see: (a) L. C. Da Silva-Filho, V. L. Júnior, M. G. Constantino, and G. V. J. Da Silva, *Synthesis*, 2008, 2527; (b) R. Nagarajan, S. Chitra, and P. T. Perumal, *Tetrahedron*, 2001*,* **57***,* 3419; (c) G. Babu and P. T. Perumal, *Tetrahedron*, 1999, **55***,* 4793; (d) G. Babu and P. T. Perumal, *Tetrahedron Lett.*, 1998, **39***,* 3225; (e) G. Babu and P. T. Perumal, *Tetrahedron.*, 1998, **54***,* 1627; (f) G. Babu and P. T. Perumal, *Tetrahedron Lett.*, 1997, **38***,* 5025.

6. (a) C. Mohan, G. Bhargava, A. P. S. Pannu, and M. P. Mahajan, *Tetrahedron Lett.,* 2007, **48**, 1711; (b) G. Bhargava, C. Mohan, and M. P. Mahajan, *Tetrahedron,* 2008, **64**, 3017; (c) G. Bhargava, V. Kumar, and M. P. Mahajan, *Tetrahedron Lett.,* 2007, **48**, 2365; (d) G. Bhargava, T. Saito, and M. P. Mahajan, *Synlett,* 2008*,* 983.

7. (a) D. C. Rowley, M. S. T. Hansen, D. Rhodes, C. A. Striffer, H. Ni, J. A. McCammon, F. D. Bushman, and W. Fenical, *Bioorg. Med. Chem*., 2002, **10**, 3619; (b) P. Molina, E. Aller, A. Lorenzo, P. Lopez-Cremades, I. Rioja, A. Ubeda, M. C. Terencio, and M. J. Alcaraz, *J. Med. Chem.,* 2001, **44**, 1011; (c) A. Kumar, S. Sinha, and P. M. S. Chauhan, *Bioorg. Med. Chem. Lett.,* 2002, **12**, 667; (d) J. B. Bher, T. Gourlain, A. Helimi and G. Guillerm, *Bioorg. Med. Chem. Lett.,* 2003, **13***,* 1713; (e) H. P. De Koning, M. I. Al-Salabi, A. M. Cohen, G. H. Coombs, and J. M. Wastling, *Int. J. Parasitol*., 2003, **33**, 821; (f) H. M. Hosni, W. M.

Basyouni, and H. A. El-Nahas, *J. Chem. Res.,* 1999, 646; (g) M. Botta, F. Occhionero, R. Nicoletti, P. Mastromarino, C. Conti, M. Margini, and J. Saladino, *Bioorg. Med. Chem.,* 1999, **9**, 1925.

8. (a) S. Kobayashi and S. Nagayama, *J. Am. Chem. Soc.,* 1996, **118**, 8977; (b) S. Kobayashi, H. Ishitani, and S. Nagayama, *Chem. Lett.,* 1995, **24**, 423.

9. (a) C. Massimo, E. Francesco, G. Salvatore, M. M. Carla, and R. Ornelio, *Org. Lett.,* 2005, **7**, 1331; (b) M. D. Garcia, A. J. Wilson, D. P. G. Emmerson, and P. R. Jenkins, *Chem. Commun.,* 2006, 2586.

10. K. K. Laal, M. Hekert, C. Brad, A. Bhatt, and T. David, *J. Chem. Soc., Perkin Trans. 1,* 2001, 578.